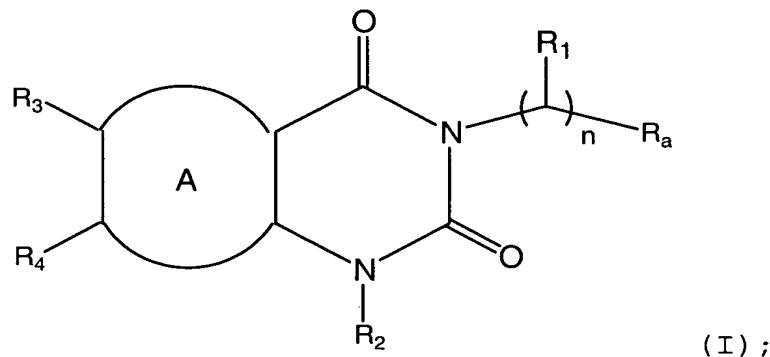


Claims:

1. A compound having formula (I):



wherein:

ring A is an optionally substituted aryl or heteroaryl ring;

R_a is -COOH;

n is 0-4;

R₁ is H, or an optionally substituted hydroxyaliphatic, aminoaliphatic, aliphatic-COOH, aliphatic-CONH₂, or arylaliphatic;

R₂ is an optionally substituted aliphatic, arylaliphatic, cycloaliphatic-aliphatic, heteroarylaliphatic, or heterocyclaliphatic;

R³ and R⁴ are independently selected from R¹¹, R¹², R¹⁴ or R¹⁵;

wherein:

each R¹¹ is independently selected from 1,2-methylenedioxy, 1,2-ethylenedioxy, R⁶ or (CH₂)_m-Y;

wherein m is 0, 1 or 2; and

Y is selected from halogen, CN, NO₂, CF₃, OCF₃, OH, SR⁶, S(O)R⁶, SO₂R⁶, NH₂, NHR⁶, N(R⁶)₂, NR⁶R⁸, COOH, COOR⁶ or OR⁶;

each R¹² is independently selected from (C₁-C₆)-straight or branched alkyl, or (C₂-C₆)-straight or

branched alkenyl or alkynyl; and each R¹² optionally comprises up to 2 substituents, wherein:

the first of said substituents, if present, is selected from R¹¹, R¹⁴ and R¹⁵, and

the second of said substituents, if present, is R¹¹;

each R¹⁴ is independently selected from OR¹⁵, OC(O)R⁶, OC(O)R¹⁵, OC(O)OR⁶, OC(O)OR¹⁵, OC(O)N(R⁶)₂, OP(O)(OR⁶)₂, SR⁶, SR¹⁵, S(O)R⁶, S(O)R¹⁵, SO₂R⁶, SO₂R¹⁵, SO₂N(R⁶)₂, SO₂NR¹⁵R⁶, SO₃R⁶, C(O)R¹⁵, C(O)OR¹⁵, C(O)R⁶, C(O)OR⁶, NC(O)C(O)R⁶, NC(O)C(O)R¹⁵, NC(O)C(O)OR⁶, NC(O)C(O)N(R⁶)₂, C(O)N(R⁶)₂, C(O)N(OR⁶)R⁶, C(O)N(OR⁶)R¹⁵, C(NOR⁶)R⁶, C(NOR⁶)R¹⁵, N(R⁶)₂, NR⁶C(O)R¹¹, NR⁶C(O)R⁶, NR⁶C(O)R¹⁵, NR⁶C(O)OR¹⁵, NR⁶C(O)N(R⁶)₂, NR⁶C(O)NR¹⁵R⁶, NR⁶SO₂R⁶, NR⁶SO₂R¹⁵, NR⁶SO₂N(R⁶)₂, NR⁶SO₂NR¹⁵R⁶, N(OR⁶)R⁶, N(OR⁶)R¹⁵, P(O)(OR⁶)N(R⁶)₂, and P(O)(OR⁶)₂;

each R¹⁵ is a cycloaliphatic, aryl, heterocyclyl, or heteroaromatic; and each R¹⁵ optionally comprises up to 3 substituents, each of which, if present, is R¹¹;

each R⁶ is independently selected from H, (C₁-C₆)-straight or branched alkyl, or (C₂-C₆) straight or branched alkenyl; and each R⁶ optionally comprises a substituent that is R⁷;

R⁷ is a cycloaliphatic, aryl, heterocyclyl, or heteroaromatic; and each R⁷ optionally comprises up to 2 substituents independently chosen from H, (C₁-C₆)-straight or branched alkyl, (C₂-C₆) straight or branched alkenyl, 1,2-methylenedioxy, 1,2-ethylenedioxy, or (CH₂)_p-Z;

wherein p is 0, 1 or 2; and

Z is selected from halogen, CN, NO₂, CF₃, OCF₃, OH, S(C₁-C₆)-alkyl, SO(C₁-C₆)-alkyl, SO₂(C₁-C₆)-alkyl, NH₂, NH(C₁-C₆)-alkyl, N((C₁-C₆)-alkyl)₂, N((C₁-C₆)-alkyl)R⁸, COOH, C(O)O(C₁-C₆)-alkyl or O(C₁-C₆)-alkyl; and

R⁸ is an amino protecting group;
provided that:

R³ and R⁴ are not simultaneously hydrogen;
when R³ is H, then R⁴ is not chloro; and
when R⁴ is H, then R³ is not -SCH₃ or -NH-C(O)CH₃.

2. The compound according to claim 1, wherein ring A is an optionally substituted 5 or 6 membered aryl or heteroaryl ring, wherein said heteroaryl ring contains up to 2 ring heteroatoms independently selected from O, S, or NH.

3. The compound according to claim 2, wherein ring A is phenyl.

4. The compound according to claim 1, wherein R₁ is hydrogen, -(CH₂)_q-X, wherein q is 1-4, and X is OH, NH₂, COOH or CONH₂, (C₁-C₆)-alkyl, or benzyl.

5. The compound according to claim 4, wherein R₁ is hydrogen, hydroxymethyl, methyl, -CH₂COOH, -CH₂CONH₂, aminobutyl, methyl, or isopentyl.

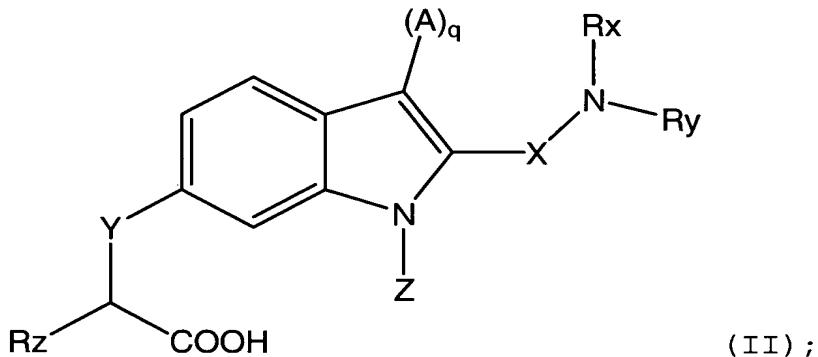
6. The compound according to claim 1, wherein R₂ is selected from butyl, isobutyl, methoxypropyl, cyclopentyl, cyclohexylmethyl, phenyl, trifluorophenyl, benzyl, fluorobenzyl, methylenedioxybenzyl, pyridylmethyl, furanylmethyl, tetrahydrofuranylmethyl, N-

morpholinylmethyl, thienylmethyl, 2-oxo-pyrrolodinylpropyl, phenylethyl, chlorophenylethyl, methoxyphenylethyl, or dimethoxyphenylethyl.

7. The compound according to claim 6, wherein R_2 is selected from 2-furanylmethyl or methyl.

According to another preferred embodiment, R_3 and R_4 are independently selected from hydrogen, halo, acetamido, allyloxy, thiophenyl, sulfoxyalkyl, or sulfoxyphenyl.

8. A compound of formula (II):



wherein:

X is $-(CH_2)_n-$, or $-C(O)-$;

n is 1-3;

Y is O, S, NH, or N(C₁-C₆ aliphatic);

Z is H or C₁-C₆ aliphatic;

Q is 0 or 1;

A , R^X , R^Y , and R^Z are independently selected from R^{11} , R^{12} , R^{14} or R^{15} ;

wherein:

each R^{11} is independently selected from 1,2-methylenedioxy, 1,2-ethylenedioxy, R^6 or $(CH_2)_m-Y$;
 wherein m is 0, 1 or 2; and
 Y is selected from halogen, CN, NO₂, CF₃, OCF₃, OH, SR⁶, S(O)R⁶, SO₂R⁶, NH₂, NHR⁶, N(R⁶)₂, NR⁶R⁸, COOH, COOR⁶ or OR⁶;

each R^{12} is independently selected from (C_1-C_6)-straight or branched alkyl, or (C_2-C_6)-straight or branched alkenyl or alkynyl; and each R^{12} optionally comprises up to 2 substituents, wherein:

the first of said substituents, if present, is selected from R^{11} , R^{14} and R^{15} , and

the second of said substituents, if present, is R^{11} ,

each R^{14} is independently selected from OR^{15} , $OC(O)R^6$, $OC(O)R^{15}$, $OC(O)OR^6$, $OC(O)OR^{15}$, $OC(O)N(R^6)_2$, $OP(O)(OR^6)_2$, SR^6 , SR^{15} , $S(O)R^6$, $S(O)R^{15}$, SO_2R^6 , SO_2R^{15} , $SO_2N(R^6)_2$, $SO_2NR^{15}R^6$, SO_3R^6 , $C(O)R^{15}$, $C(O)OR^{15}$, $C(O)R^6$, $C(O)OR^6$, $NC(O)C(O)R^6$, $NC(O)C(O)R^{15}$, $NC(O)C(O)OR^6$, $NC(O)C(O)N(R^6)_2$, $C(O)N(R^6)_2$, $C(O)N(OR^6)R^6$, $C(O)N(OR^6)R^{15}$, $C(NOR^6)R^6$, $C(NOR^6)R^{15}$, $N(R^6)_2$, $NR^6C(O)R^{11}$, $NR^6C(O)R^6$, $NR^6C(O)R^{15}$, $NR^6C(O)OR^6$, $NR^6C(O)OR^{15}$, $NR^6C(O)N(R^6)_2$, $NR^6C(O)NR^{15}R^6$, $NR^6SO_2R^6$, $NR^6SO_2R^{15}$, $NR^6SO_2N(R^6)_2$, $NR^6SO_2NR^{15}R^6$, $N(OR^6)R^6$, $N(OR^6)R^{15}$, $P(O)(OR^6)N(R^6)_2$, and $P(O)(OR^6)_2$;

each R^{15} is a cycloaliphatic, aryl, heterocyclyl, or heteroaromatic; and each R^{15} optionally comprises up to 3 substituents, each of which, if present, is R^{11} ;

each R^6 is independently selected from H, (C_1-C_6)-straight or branched alkyl, or (C_2-C_6) straight or branched alkenyl; and each R^6 optionally comprises a substituent that is R^7 ;

R^7 is a cycloaliphatic, aryl, heterocyclyl, or heteroaromatic; and each R^7 optionally comprises up to 2 substituents independently chosen from H, (C_1-C_6)-straight or branched alkyl, (C_2-C_6) straight or branched alkenyl, 1,2-methylenedioxy, 1,2-ethylenedioxy, or $(CH_2)_p-Z$;

wherein p is 0, 1 or 2; and
Z is selected from halogen, CN, NO₂, CF₃, OCF₃, OH,
S(C₁-C₆)-alkyl, SO(C₁-C₆)-alkyl, SO₂(C₁-C₆)-alkyl, NH₂,
NH(C₁-C₆)-alkyl, N((C₁-C₆)-alkyl)₂, N((C₁-C₆)-alkyl)R⁸,
COOH, C(O)O(C₁-C₆)-alkyl or O(C₁-C₆)-alkyl; and

R⁸ is an amino protecting group;
or R^x and R^y, taken together, form an optionally
substituted heterocyclic ring having up to 3
substituents.

9. A pharmaceutical composition comprising a compound according to any one of claims 1-8 and a pharmaceutically acceptable adjuvant or carrier.

10. A method for treating or lessening the severity of a disease in a patient, wherein said disease is selected from autoimmune diseases, proliferative diseases, angiogenic disorders, or cancers, said method comprising the step of administering to said patient a composition according to claim 9.

11. A method for treating or lessening the severity of a SHP-2-mediated disease or condition in a patient comprising the step of administering to said patient a composition according to claim 9.

12. The method according to claim 10, wherein said autoimmune disease is selected from glomerulo-nephritis, rheumatoid arthritis, systemic lupus erythematosus, scleroderma, chronic thyroiditis, Graves' disease, autoimmune gastritis, diabetes, autoimmune hemolytic anemia, autoimmune neutropenia, thrombocytopenia, atopic dermatitis, chronic active hepatitis, myasthenia gravis, multiple sclerosis, inflammatory bowel disease,

ulcerative colitis, Crohn's disease, psoriasis, or graft vs. host disease.

13. The method according to claim 10, wherein said proliferative disease is selected from acute myelogenous leukemia, chronic myelogenous leukemia, metastatic melanoma, Kaposi's sarcoma, multiple myeloma or HTLV-1-mediated tumorigenesis.

14. The method according to claim 10, wherein said angiogenic disorder is selected from solid tumors, ocular neovascularization, or infantile haemangiomas.

15. The method according to claim 10, wherein said cancers is selected from colon cancer, breast cancer, stomach cancer, or ovarian cancers.

16. An implantable medical device coated with a compound according to any one of claims 1-8, wherein said device is selected from prostheses, artificial valves, vascular grafts, stents or catheters.